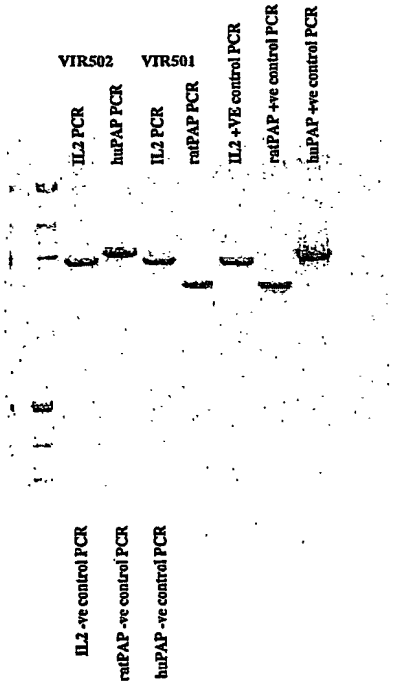


FIGURE 1

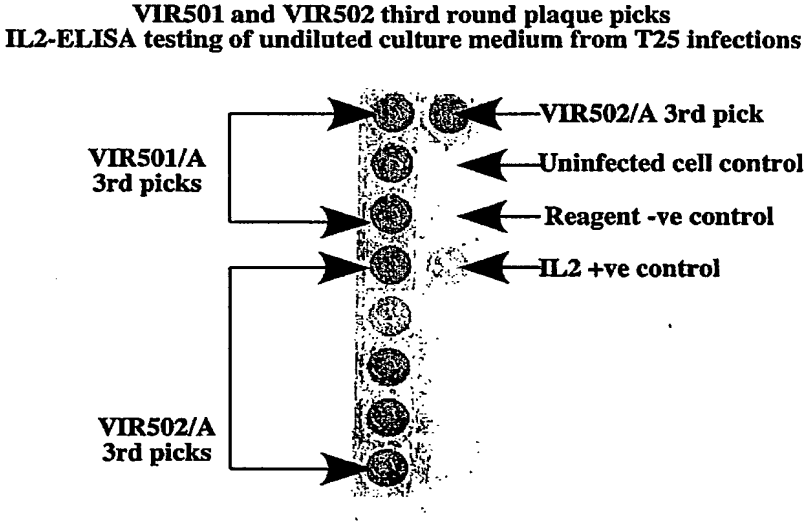


FIGURE 2

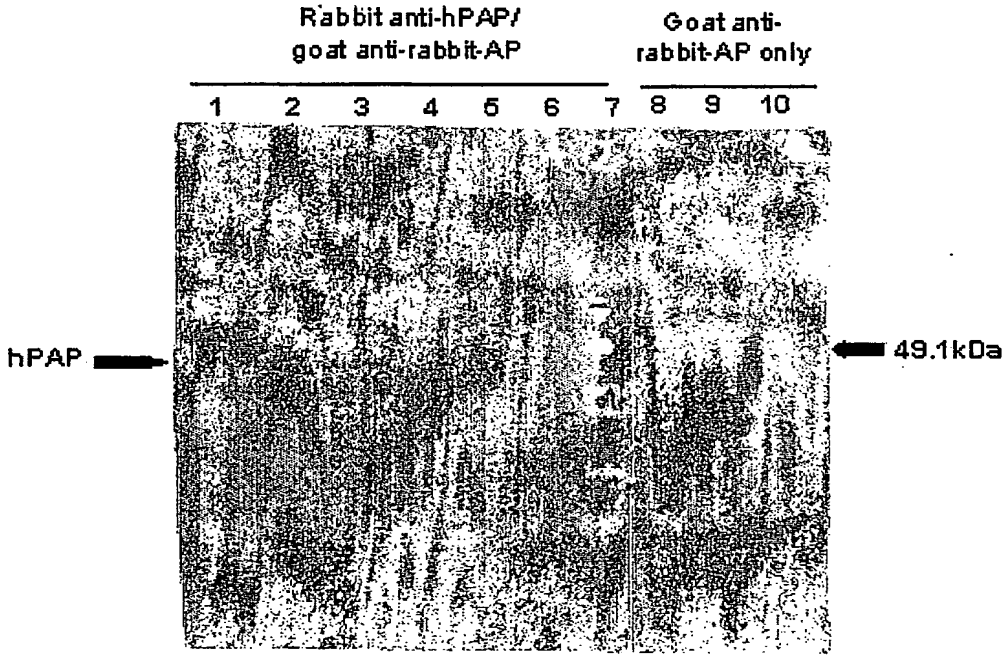


FIGURE 3

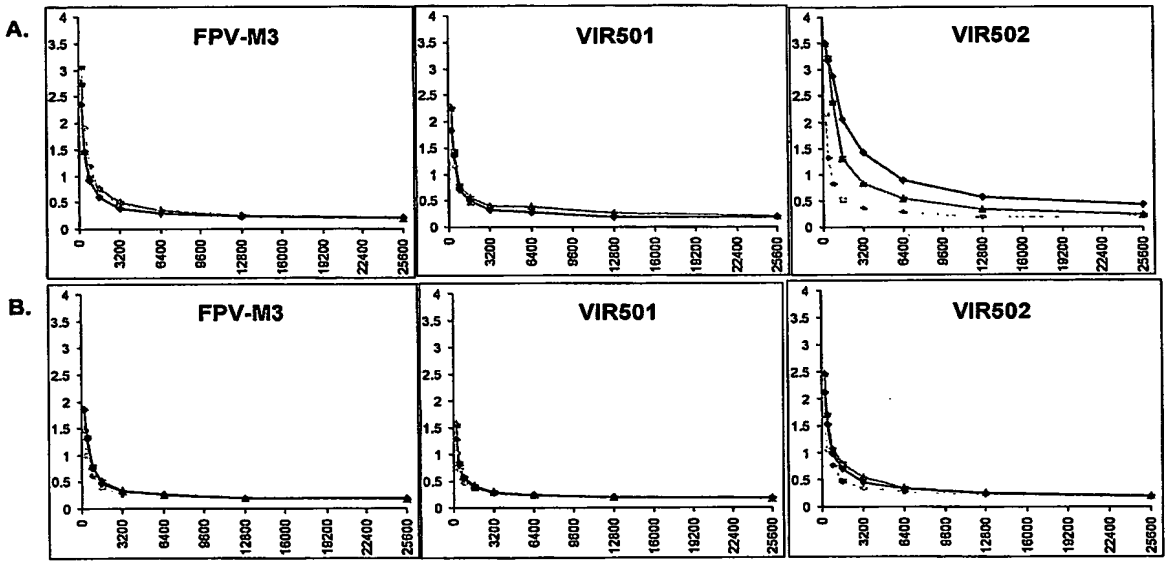

A.
FPV-M3
VIR501
VIR502
B.
FPV-M3
VIR501
VIR502
0
0.5
1
1.5
2
2.5
3
3.5
4
0
3200
6400
9600
12800
16000
19200
22400
25600

FIGURE 4

Insertion site of VIR501 containing human IL2 and rat PAP sequences

The FPV ORFs are with reference to FPV genome ORFs – Genbank Ac No.: AF198100

ATGGATAGAAATATCAATTTTAGTCCTGTATTTATAGAACCTAGGTTTAAACACGAGTTTCTATTATCTCCTCAAAGGTATTTT
TACCTATCTTTATAGTTAAAATCAGGACATAAATATCTTGGATCCAAATTTGTGCTCAAAGATAATAGAGGAGTTTCCATAAAA

TATATATTAGTTTTTGAAGTAATAGTAGCTTTGATTATATTGAATTTTTTCTTTAAGGAAGAAATATTATATACATTTTTTCCG
ATATATAATCAAAAACTTCATTATCATCGAAACTAATATAACTTAAAAAAGAAATTCCTTCTTTATAATATATGTAAAAAAGGC
FPV132R ORF in bold →

TTAGCTAAGCCTTCTAAAAATTCAATAAATAGTCTGCTGGATAGAACTATGTTAAAATGTGAAGAAGATGGATCTTTGATGATT
AATCGATTCGGAAGATTTTTAAGTTATTTATCAGACGACCTATCTTGATACAATTTTACACTTCTTCTACCTAGAAACTACTAA

TCGAGACCTTCCGGTATCTATTCGGCCTTGAGTTTAGATGGTTCACCGGTAAGGATTTCCGATTGTAGTTTGCTTTTATCGTCA
AGCTCTGGAAGGCCATAGATAAGCCGGAACTCAAATCTACCAAGTGGCCATTCCTAAAGGCTAACATCAAACGAAAATAGCAGT

ATAAATGGCGCATCCTCATCAACATCTCCTTACTCTATTTTTAACAGACGATAACGGATTTTATTCTTATCTATCCGAAAAAAG
TATTTACCGCGTAGGAGTAGTTGTAGAGGAATGAGATAAAAATTGTCTGCTATTGCCTAAAATAAGAATAGATAGGCTTTTTTC

TGATGATGAAGCTCTTGAAGACATAAATACTATTAAGAAATATATGGACTTTATTCTAAGCGTTCTTATACGTTCTAAAGAGAA
ACTACTACTTCGAGAACTTCTGTATTTATGATAATTCTTTATATACCTGAAATAAGATTCGCAAGAATATGCAAGATTTCTCTT

ACTAGAAAATATAGGATGTTCTTACGAGCCTATGAGTGAATCGTTTAAGGCTCTTATTAAAGTAAAGGATGATGGTACTTTAGT
TGATCTTTTATATCCTACAAGAATGCTCGGATACTCACTTAGCAAATTCCGAGAATAATTTCATTTCCTACTACCATGAAATCA

AAAAGCATTTACCAAGCCATTGTTAAATCCTCATTCCGAAAAGATAGTTTTAGATAGAGGTTATACTTCGGATTTTGCTATAAG
TTTTCGTAAATGGTTCGGTAACAATTTAGGAGTAAGGCTTTTCTATCAAAATCTATCTCCAATATGAAGCCTAAAACGATATTC

CGTAATAAGACTATCTAGTAAAAGCAGTTATATACTTCCCGCAAATACAAAATACATAAATCCAAACGAGAATATGTATATAAA
GCATTATTCTGATAGATCATTTTCGTCAATATATGAAGGGCGTTTATGTTTTATGTATTTAGGTTTGCTCTTATACATATATTT

CAACCTAATATCACTACTGAAGCGCAACTAGATCT***TCCAAACCCACCCGCTTTTTATAGTAAGTTTTTCACCCATAAATAATAA***
GTTGGATTATAGTGATGACTTCGCGTTGATCTAG***AAGGTTTGGGTGGGCGAAAAATATCATTCAAAAAGTGGGTATTTATTATT***
vaccinia p7.5 promoter in bold & italic →

ATACAATAATTAATTTCTCGTAAAAGTAGAAAATATATTCTAATTTATTGCACGGTCTAGAACTAGTGgatccATGTACAGGAT
TATGTTATTAATTAAAGAGCATTTTCATCTTTTATATAAGATTAAATAACGTGCCAGATCTTGATCACctaggTACATGTCCTA
> M Y R M

GCAACTCCTGTCTTGCATTGCACTAATTCTTGCACTTGTCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAA
CGTTGAGGACAGAACGTAACGTGATTAAGAACGTGAACAGTGTTTGTCACGTGGATGAAGTTCAAGCTGTTTCTTTTGTTTCTT
> Q L L S C I A L I L A L V T N S A P T S S S T K K T K K
human IL2 protein coding sequence →

AACACAGCTACAACTGGAGCATTTACTGCTGGATTTACAGATGATTTTGAATGGAATTAATAATTACAAGAATCCCAAACTCAC
TTGTGTCGATGTTGACCTCGTAAATGACGACCTAAATGTCTACTAAAACTTACCTTAATTATTAATGTTCTTAGGGTTTGAGTG
> T Q L Q L E H L L L D L Q M I L N G I N N Y K N P K L T

CAGGATGCTCACATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACAGCTTCAGTGTCTAGAAGAAGAACTCAAACC
GTCCTACGAGTGTAAATTCAAAATGTACGGGTTCTTCCGGTGTCTTGACTTTGTCGAAGTCACAGATCTTCTTCTTGAGTTTGG
> R M L T F K F Y M P K K A T E L K Q L Q C L E E E L K P

TCTGGAGGAAGTGCTGAATTTAGCTCAAAGCAAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAATATCAACGTAATAGT
AGACCTCCTTCACGACTTAAATCGAGTTTCGTTTTTGAAAGTGAATTCTGGGTCCCTGAATTAGTCGTTATAGTTGCATTATCA
> L E E V L N L A Q S K N F H L R P R D L I S N I N V I V

TCTGGAACTAAAGGGATCTGAAACAACATTCATGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAACAGATG
AGACCTTGATTTCCCTAGACTTTGTTGTAAGTACACACTTATACGTCTACTCTGTCGTTGGTAACATCTTAAAGACTTGTCTAC
> L E L K G S E T T F M C E Y A D E T A T I V E F L N R W

FIGURE 5

GATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGA**TTTTTGT**aGATCTGTCGAC***CATTTAGTATCCTAAAATTGAA***
CTAATGGAAAACAGTTTCGTAGTAGAGTTGTGATTGAACT**AAAAACA**tCTAGACAGCTG***GTAAATCATAGGATTTTAACTT***
> I T F C Q S I I S T L T • FPV early/late promoter

Early transcriptional
stop sequence (bold)

TTGTAATTATCGATAATAAATGAGAGCTGTCCCTCTGCACCTCGTCGGGACAGCAAGCCTCACCCTTGGCTTCTTGCTCCTGCT
AACATTAATAGCTATTATTTACTCTCGACAGGGAGACGTGGAGCAGCCCTGTCGTTCGGAGTGGGAACCGAAGAACGAGGACGA
> M R A V P L H L V G T A S L T L G F L L L L

Rat PAP protein coding sequence

ATCTCTCCGCCTGGACCCAGGCCAAGCCAAGGAGTTGAAGTTTGTGACATTGGTGTTCCGGCATGGAGACCGAGGTCCCATCGA
TAGAGAGGCGGACCTGGGTCCGGTTCGGTTCCTCAACTTCAAACACTGTAACCACAAGGCCGTACCTCTGGCTCCAGGGTAGCT
> S L R L D P G Q A K E L K F V T L V F R H G D R G P I E

GACCTTTCCTAATGACCCCATTAAGGAATCCTCGTGGCCACAAGGATTTGGCCAACTCACCAAGTGGGGCATGGGACAGCACTA
CTGGAAAGGATTACTGGGGTAATTCCTTAGGAGCACCGGTGTTCCTAAACCGGTTGAGTGGTTCACCCCGTACCCTGTCGTGAT
> T F P N D P I K E S S W P Q G F G Q L T K W G M G Q H Y

CGAACTCGGAAGTTATATAAGGAGAAGATACGGGAGATTCTTGAACAACTCCTATAAACATGACCAGGTTTATATCCGAAGCAC
GCTTGAGCCTTCAATATATTCCTCTTCTATGCCCTCTAAGAACTTGTTGAGGATATTTGTACTGGTCCAAATATAGGCTTCGTG
> E L G S Y I R R R Y G R F L N N S Y K H D Q V Y I R S T

AGATGTTGACAGGACTCTGATGAGCGCTATGACAAACCTCGCAGCCCTGTTTCCCCCTGAGGGGATCAGCATCTGGAATCCCAG
TCTACAACTGTCCTGAGACTACTCGCGATACTGTTTGGAGCGTCGGGACAAAGGGGGACTCCCCTAGTCGTAGACCTTAGGGTC
> D V D R T L M S A M T N L A A L F P P E G I S I W N P R

ACTGCTCTGGCAGCCCATCCCAGTGCACACCGTGTCTCTCTCTGAGGATCGGTTGCTATACCTGCCTTTCAGGGACTGTCCTCG
TGACGAGACCGTCGGGTAGGGTCACGTGTGGCACAGAGAGAGACTCCTAGCCAACGATATGGACGGAAAGTCCCTGACAGGAGC
> L L W Q P I P V H T V S L S E D R L L Y L P F R D C P R

CTTTCAAGAACTCAAGAGTGAGACTTTAAAATCTGAGGAGTTCCTGAAGAGGCTTCAACCATATAAAAGCTTCATAGACACCTT
GAAAGTTCTTGAGTTCTCACTCTGAAATTTTAGACTCCTCAAGGACTTCTCCGAAGTTGGTATATTTTCGAAGTATCTGTGGAA
> F Q E L K S E T L K S E E F L K R L Q P Y K S F I D T L

GCCATCGCTGTCGGGATTCGAGGACCAGGATCTTTTTGAAATCTGGAGTAGGCTTTACGACCCTTTATATTGCGAGAGTGTTCA
CGGTAGCGACAGCCCTAAGCTCCTGGTCCTAGAAAAACTTTAGACCTCATCCGAAATGCTGGGAAATATAACGCTCTCACAAGT
> P S L S G F E D Q D L F E I W S R L Y D P L Y C E S V H

CAATTTCACCTTCCGCACCTGGGCCACAGAGGACGCCATGACTAAGTTGAAGGAGTTGTCAGAATTATCTCTGTTATCTCTTTA
GTTAAAGTGGAAGGCGTGGACCCGGTGTCTCCTGCGGTACTGATTCAACTTCCTCAACAGTCTTAATAGAGACAATAGAGAAAT
> N F T F R T W A T E D A M T K L K E L S E L S L L S L Y

TGGAATTCACAAGCAGAAAGAGAAATCTAGACTCCAGGGGGGCGTCCTGGTCAATGAAATTCTCAAGAACATGAAGCTTGCAAC
ACCTTAAGTGTTCGTCTTTCTCTTTAGATCTGAGGTCCCCCCGCAGGACCAGTTACTTTAAGAGTTCTTGTACTTCGAACGTTG
> G I H K Q K E K S R L Q G G V L V N E I L K N M K L A T

TCAACCACAGAAGGCCAGGAAGTTGATCATGTATTCTGCATATGACACTACTGTGAGTGGCCTGCAGATGGCGCTAGAGCTTTA
AGTTGGTGTCTTCCGGTCCTTCAACTAGTACATAAGACGTATACTGTGATGACACTCACCGGACGTCTACCGCGATCTCGAAAT
> Q P Q K A R K L I M Y S A Y D T T V S G L Q M A L E L Y

TAATGGACTTCTACCTCCCTACGCTTCCTGCCACATAATGGAATTGTACCAGGATAATGGGGGGACCTTCGTGGAGATGTACTA
ATTACCTGAAGATGGAGGGATGCGAAGGACGGTGTATTACCTTAACATGGTCCTATTACCCCCCTGGAAGCACCTCTACATGAT
> N G L L P P Y A S C H I M E L Y Q D N G G T F V E M Y Y

CCGGAATGAGACCCAGAACGAGCCCTACCCACTCACGCTGCCGGGCTGTACCCACAGCTGCCCTCTGGAGAAGTTTGCAGAGCT
GGCCTTACTCTGGGTCTTGCTCGGGATGGGTGAGTGCGACGGCCCGACATGGGTGTCGACGGGAGACCTCTTCAAACGTCTCGA
> R N E T Q N E P Y P L T L P G C T H S C P L E K F A E L

FIGURE 5 cont.

ACTGGACCCCGTGATCCCCCAGGACTGGGCCACAGAGTGTATGGGCACAAGCAACCACCAAGCGTCGCTGTAATTTTTCTGTCG
TGACCTGGGGCACTAGGGGGTCCTGACCCGGTGTCTCACATACCCGTGTTCGTTGGTGGTTCGCAGCGACATTAAAAAGACAGC
> L D P V I P Q D W A T E C M G T S N H Q A S L •

ACCCATGGTTGTTAAAAAGGAATTGAAAGAAAATATTTTATATCGTAATAAATTAAATATGCATGAAGGACATCAGGAGTCTTT
TGGGTACCAACAATTTTTCCTTAACTTTCTTTTATAAAATATAGCATTATTTAATTTATACGTACTTCCTGTAGTCCTCAGAAA
FPV134R ORF in bold

TAAAGAACTTGAAATGACAAAACCTTATATGTTCTTCAATGAACTAGTAGGTGAAGAAGACTATAACAAAGAGTTAGAAAATTC
ATTTCTTGAACTTTACTGTTTTGGAATATACAAGAAGTTACTTGATCATCCACTTCTTCTGATATTGTTTCTCAATCTTTTAAG

TAATACTAAGTTTCAAGGACAGGGCCAGCTTAAGCTGTTATTAGGAGAACTTTATTTCTTAAATACATTAATCAAGAATAAAAC
ATTATGATTCAAAGTTCCTGTCCCGGTCGAATTCGACAATAATCCTCTTGAAATAAAGAATTTATGTAATTAGTTCTTATTTTG

GTTATGTTCAGATACAGTTATCGTGTATATAGGGTCAGCACCAGGAAGCCATATAAATTTTTTTATATCATTATATGGATGA
CAATACAAGTCTATGTCAATAGCACATATATCCCAGTCGTGGTCCTTCGGTATATTTAAAAAATATAGTAATATACCTACT
Early transcriptional
stop sequence for rat PAP

TCTTAAAATAGATTTAAAATGGATATTAATAGATGGTAGAGATCATGATCGATCTCTAGAAAGTCTTAAAAATGTGTCTATAAT
AGAATTTTATCTAAATTTTACCTATAATTATCTACCATCTCTAGTACTAGCTAGAGATCTTTCAGAATTTTTACACAGATATTA

ACATAGGTTTGTAGATGAACAATACTTGTTTAAGCTACGTAATATGATTAGGAAAAACCATAAAATTGTACTGATATCAGATAT
TGTATCCAAACATCTACTTGTTATGAACAAATTCGATGCATTATACTAATCCTTTTTGGTATTTTAACATGACTATAGTCTATA

TAGATCGCTAAGAGGAAAAGAACCTACTAGCGAGGACCTATTACACGATTACGCGTTGCAGAATCAAATGGTAAGCATTCTTAA
ATCTAGCGATTCTCCTTTTCTTGGATGATCGCTCCTGGATAATGTGCTAATGCGCAACGTCTTAGTTTACCATTCGTAAGAATT

ACCAATAGCATCGAGCCTGAAATGGAGATGTCCGTTTCCGGATCAGTGGATAAGAGACTTTTACATTCCTTGTGGAGATGAGTT
TGGTTATCGTAGCTCGGACTTTACCTCTACAGGCAAAGGCCTAGTCACCTATTCTCTGAAAATGTAAGGAACACCTCTACTCAA

T
A

FIGURE 5 cont.

Insertion site of VIR502 containing human IL2 and human PAP sequences

The FPV ORFs are with reference to FPV genome ORFs – Genbank Ac No.: AF198100

ATGGATAGAAATATCAATTTTAGTCCTGTATTTATAGAACCTAGGTTTAAACACGAGTTTCTATTATCTCCTCAAAGGTA
TACCTATCTTTATAGTTAAAATCAGGACATAAATATCTTGGATCCAAATTTGTGCTCAAAGATAATAGAGGAGTTTCCAT
FPV132R ORF in bold →

TTTTTATATATTAGTTTTTGAAGTAATAGTAGCTTTGATTATATTGAATTTTTTCTTTAAGGAAGAAATATTATATACAT
AAAAATATATAATCAAAAACTTCATTATCATCGAAACTAATATAACTTAAAAAAGAAATTCCTTCTTTATAATATATGTA

TTTTTCCGTTAGCTAAGCCTTCTAAAAATTCAATAAATAGTCTGCTGGATAGAACTATGTTAAAATGTGAAGAAGATGGA
AAAAAGGCAATCGATTCGGAAGATTTTTAAGTTATTTATCAGACGACCTATCTTGATACAATTTTACACTTCTTCTACCT

TCTTTGATGATTTCGAGACCTTCCGGTATCTATTCGGCCTTGAGTTTAGATGGTTCACCGGTAAGGATTTCCGATTGTAG
AGAAACTACTAAAGCTCTGGAAGGCCATAGATAAGCCGGAACTCAAATCTACCAAGTGGCCATTCCTAAAGGCTAACATC

TTTGCTTTTATCGTCAATAAATGGCGCATCCTCATCAACATCTCCTTACTCTATTTTTAACAGACGATAACGGATTTTAT
AAACGAAAATAGCAGTTATTTACCGCGTAGGAGTAGTTGTAGAGGAATGAGATAAAAATTGTCTGCTATTGCCTAAAATA

TCTTATCTATCCGAAAAAAGTGATGATGAAGCTCTTGAAGACATAAATACTATTAAGAAATATATGGACTTTATTCTAAG
AGAATAGATAGGCTTTTTTCACTACTACTTCGAGAACTTCTGTATTTATGATAATTCTTTATATACCTGAAATAAGATTC

CGTTCTTATACGTTCTAAAGAGAAACTAGAAAATATAGGATGTTCTTACGAGCCTATGAGTGAATCGTTTAAGGCTCTTA
GCAAGAATATGCAAGATTTCTCTTTGATCTTTTATATCCTACAAGAATGCTCGGATACTCACTTAGCAAATTCCGAGAAT

TTAAAGTAAAGGATGATGGTACTTTAGTAAAAGCATTTACCAAGCCATTGTTAAATCCTCATTCCGAAAAGATAGTTTTA
AATTTCATTTCCTACTACCATGAAATCATTTTCGTAAATGGTTCGGTAACAATTTAGGAGTAAGGCTTTTCTATCAAAAT

GATAGAGGTTATACTTCGGATTTTGCTATAAGCGTAATAAGACTATCTAGTAAAAGCAGTTATATACTTCCCGCAAATAC
CTATCTCCAATATGAAGCCTAAAACGATATTCGCATTATTCTGATAGATCATTTTCGTCAATATATGAAGGGCGTTTATG

AAAATACATAAATCCAAACGAGAATATGTATATAAACAACCTAATATCACTACTGAAGCGCAACTAGATCT***TCCAAACCC***
TTTTATGTATTTAGGTTTGCTCTTATACATATATTTGTTGGATTATAGTGATGACTTCGCGTTGATCTAGA***AGGTTTGGG***

ACCCGCTTTTTATAGTAAGTTTTTCACCCA*TAAATAATAAATACAATAATTAATTTCTCGTAAAAGTAGAAAATATATTC*
TGGGCG*AAAAATATCATTCAAAAAGTGGGTATTTATTATTTATGTTATTAATTAAAGAGCATTTTCATCTTTTATATAAG*
vaccinia p7.5 promoter in bold & italic →

TAATTTATTGCACGGTCTAGAACTAGTGgatccATGTACAGGATGCAACTCCTGTCTTGCATTGCACTAATTCTTGCACT
ATTAAATAACGTGCCAGATCTTGATCACctaggTACATGTCCTACGTTGAGGACAGAACGTAACGTGATTAAGAACGTGA
> M Y R M Q L L S C I A L I L A L
Human IL2 protein coding sequence →

TGTCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAAAACACAGCTACAACTGGAGCATTTACTGCTGG
ACAGTGTTTGTCACGTGGATGAAGTTCAAGCTGTTTCTTTTGTTTCTTTTGTGTCGATGTTGACCTCGTAAATGACGACC
> V T N S A P T S S S T K K T K K T Q L Q L E H L L L

ATTTACAGATGATTTTGAATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCACATTTAAGTTTTACATG
TAAATGTCTACTAAAACTTACCTTAATTATTAATGTTCTTAGGGTTTGAGTGGTCCTACGAGTGTAAATTCAAAATGTAC
>D L Q M I L N G I N N Y K N P K L T R M L T F K F Y M

CCCAAGAAGGCCACAGAACTGAAACAGCTTCAGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTAGC
GGGTTCTTCCGGTGTCTTGACTTTGTCGAAGTCACAGATCTTCTTCTTGAGTTTGGAGACCTCCTTCACGACTTAAATCG
> P K K A T E L K Q L Q C L E E E L K P L E E V L N L A

TCAAAGCAAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAATATCAACGTAATAGTTCTGGAACTAAAGGGATCTG
AGTTTCGTTTTTGAAAGTGAATTCTGGGTCCCTGAATTAGTCGTTATAGTTGCATTATCAAGACCTTGATTTCCCTAGAC
> Q S K N F H L R P R D L I S N I N V I V L E L K G S

FIGURE 6

```
AAACAACATTCATGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAACAGATGGATTACCTTTTGTCAA
TTTGTTGTAAGTACACACTTATACGTCTACTCTGTCGTTGGTAACATCTTAAAGACTTGTCTACCTAATGGAAAACAGTT
>E  T  T  F  M  C  E  Y  A  D  E  T  A  T  I  V  E  F  L  N  R  W  I  T  F  C  Q

AGCATCATCTCAACACTAACTTGATTTTTTGTaGATCTGtcgaccatttagtatcctaaaattgaattgtaattatcg
TCGTAGTAGAGTTGTGATTGAACTAAAAAACAtCTAGACagctggtaaatcataggattttaacttaacattaatagc
>  S  I  I  S  T  L  T  •                                  FPV early late promoter →
                         Early transcriptional      in bold & italic
                         stop sequence in bold

ataataaATGAGAGCTGCACCCCTCCTCCTGGCCAGGGCAGCAAGCCTTAGCCTTGGCTTCTTGTTTCTGCTTTTTTTCT
tattattTACTCTCGACGTGGGGAGGAGGACCGGTCCCGTCGTTCGGAATCGGAACCGAAGAACAAAGACGAAAAAAAGA
      >  M  R  A  A  P  L  L  L  A  R  A  A  S  L  S  L  G  F  L  F  L  L  F  F
           Human PAP protein coding sequence →

GGCTAGACCGAAGTGTACTAGCCAAGGAGTTGAAGTTTGTGACTTTGGTGTTTCGGCATGGAGACCGAAGTCCCATTGAC
CCGATCTGGCTTCACATGATCGGTTCCTCAACTTCAAACACTGAAACCACAAAGCCGTACCTCTGGCTTCAGGGTAACTG
>W  L  D  R  S  V  L  A  K  E  L  K  F  V  T  L  V  F  R  H  G  D  R  S  P  I  D

ACCTTTCCCACTGACCCCATAAAGGAATCCTCATGGCCACAAGGATTTGGCCAACTCACCCAGCTGGGCATGGAGCAGCA
TGGAAAGGGTGACTGGGGTATTTCCTTAGGAGTACCGGTGTTCCTAAACCGGTTGAGTGGGTCGACCCGTACCTCGTCGT
>  T  F  P  T  D  P  I  K  E  S  S  W  P  Q  G  F  G  Q  L  T  Q  L  G  M  E  Q  H

TTATGAACTTGGAGAGTATATAAGAAAGAGATATAGAAAATTCTTGAATGAGTCCTATAAACATGAACAGGTTTATATTC
AATACTTGAACCTCTCATATATTCTTTCTCTATATCTTTTAAGAACTTACTCAGGATATTTGTACTTGTCCAAATATAAG
>  Y  E  L  G  E  Y  I  R  K  R  Y  R  K  F  L  N  E  S  Y  K  H  E  Q  V  Y  I

GAAGCACAGACGTTGACCGGACTTTGATGAGTGCTATGACAAACCTGGCAGCCCTGTTTCCCCCAGAAGGTGTCAGCATC
CTTCGTGTCTGCAACTGGCCTGAAACTACTCACGATACTGTTTGGACCGTCGGGACAAAGGGGGTCTTCCACAGTCGTAG
>R  S  T  D  V  D  R  T  L  M  S  A  M  T  N  L  A  A  L  F  P  P  E  G  V  S  I

TGGAATCCTATCCTACTCTGGCAGCCCATCCCGGTGCACACAGTTCCTCTTTCTGAAGATCAGTTGCTATACCTGCCTTT
ACCTTAGGATAGGATGAGACCGTCGGGTAGGGCCACGTGTGTCAAGGAGAAAGACTTCTAGTCAACGATATGGACGGAAA
>  W  N  P  I  L  L  W  Q  P  I  P  V  H  T  V  P  L  S  E  D  Q  L  L  Y  L  P  F

CAGGAACTGCCCTCGTTTTCAAGAACTTGAGAGTGAGACTTTGAAATCAGAGGAATTCCAGAAGAGGCTGCACCCTTATA
GTCCTTGACGGGAGCAAAAGTTCTTGAACTCTCACTCTGAAACTTTAGTCTCCTTAAGGTCTTCTCCGACGTGGGAATAT
>  R  N  C  P  R  F  Q  E  L  E  S  E  T  L  K  S  E  E  F  Q  K  R  L  H  P  Y

AGGATTTTATAGCTACCTTGGGAAAACTTTCAGGATTACATGGCCAGGACCTTTTTGGAATTTGGAGTAAAGTCTACGAC
TCCTAAAATATCGATGGAACCCTTTTGAAAGTCCTAATGTACCGGTCCTGGAAAAACCTTAAACCTCATTTCAGATGCTG
>K  D  F  I  A  T  L  G  K  L  S  G  L  H  G  Q  D  L  F  G  I  W  S  K  V  Y  D

CCTTTATATTGTGAGAGTGTTCACAATTTCACTTTACCCTCCTGGGCCACTGAGGACACCATGACTAAGTTGAGAGAATT
GGAAATATAACACTCTCACAAGTGTTAAAGTGAAATGGGAGGACCCGGTGACTCCTGTGGTACTGATTCAACTCTCTTAA
>  P  L  Y  C  E  S  V  H  N  F  T  L  P  S  W  A  T  E  D  T  M  T  K  L  R  E  L

GTCAGAATTGTCCCTCCTGTCCCTCTATGGAATTCACAAGCAGAAAGAGAAATCTAGGCTCCAAGGGGGTGTCCTGGTCA
CAGTCTTAACAGGGAGGACAGGGAGATACCTTAAGTGTTCGTCTTTCTCTTTAGATCCGAGGTTCCCCCACAGGACCAGT
>  S  E  L  S  L  L  S  L  Y  G  I  H  K  Q  K  E  K  S  R  L  Q  G  G  V  L  V

ATGAAATCCTCAATCACATGAAGAGAGCAACTCAGATACCAAGCTACAAAAAACTTATCATGTATTCTGCGCATGACACT
TACTTTAGGAGTTAGTGTACTTCTCTCGTTGAGTCTATGGTTCGATGTTTTTTGAATAGTACATAAGACGCGTACTGTGA
>N  E  I  L  N  H  M  K  R  A  T  Q  I  P  S  Y  K  K  L  I  M  Y  S  A  H  D  T

ACTGTGAGTGGCCTACAGATGGCGCTAGATGTTTACAACGGACTCCTTCCTCCCTATGCTTCTTGCCACTTGACGGAATT
TGACACTCACCGGATGTCTACCGCGATCTACAAATGTTGCCTGAGGAAGGAGGGATACGAAGAACGGTGAACTGCCTTAA
>  T  V  S  G  L  Q  M  A  L  D  V  Y  N  G  L  L  P  P  Y  A  S  C  H  L  T  E  L
```

FIGURE 6 cont.

GTACTTTGAGAAGGGGGAGTACTTTGTGGAGATGTACTATCGGAATGAGACGCAGCACGAGCCGTATCCCCTCATGCTAC
CATGAAACTCTTCCCCCTCATGAAACACCTCTACATGATAGCCTTACTCTGCGTCGTGCTCGGCATAGGGGAGTACGATG
> Y F E K G E Y F V E M Y Y R N E T Q H E P Y P L M L

CTGGCTGCAGCCCTAGCTGTCCTCTGGAGAGGTTTGCTGAGCTGGTTGGCCCTGTGATCCCTCAAGACTGGTCCACGGAG
GACCGACGTCGGGATCGACAGGAGACCTCTCCAAACGACTCGACCAACCGGGACACTAGGGAGTTCTGACCAGGTGCCTC
>P G C S P S C P L E R F A E L V G P V I P Q D W S T E

TGTATGACCACAAACAGCCATCAAGGTACTGAGGACAGTACAGATTAATTTTTCTGTCGACCCATGGTTGTTAAAAAGGA
ACATACTGGTGTTTGTCGGTAGTTCCATGACTCCTGTCATGTCTAATTAAAAAGACAGCTGGGTACCAACAATTTTTCCT
> C M T T N S H Q G T E D S T D •

ATTGAAAGAAAATATTTTATATCGTAATAAATTAAATATGCATGAAGGACATCAGGAGTCTTTTAAAGAACTTGAAATGA
TAACTTTCTTTTATAAAATATAGCATTATTTAATTTATACGTACTTCCTGTAGTCCTCAGAAAATTTCTTGAACTTTACT
FPV134 ORF in bold →

CAAAACCTTATATGTTCTTCAATGAACTAGTAGGTGAAGAAGACTATAACAAAGAGTTAGAAAATTCTAATACTAAGTTT
GTTTTGGAATATACAAGAAGTTACTTGATCATCCACTTCTTCTGATATTGTTTCTCAATCTTTTAAGATTATGATTCAAA

CAAGGACAGGGCCAGCTTAAGCTGTTATTAGGAGAACTTTATTTCTTAAATACATTAATCAAGAATAAAACGTTATGTTC
GTTCCTGTCCCGGTCGAATTCGACAATAATCCTCTTGAAATAAAGAATTTATGTAATTAGTTCTTATTTTGCAATACAAG

AGATACAGTTATCGTGTATATAGGGTCAGCACCAGGAAGCCATATAAATTTTTTATATCATTATATGGATGATCTTA
TCTATGTCAATAGCACATATATCCCAGTCGTGGTCCTTCGGTATATTTAAAAAATATAGTAATATACCTACTAGAAT
Early transcriptional
stop sequence in bold
for human PAP sequence

AAATAGATTTAAAATGGATATTAATAGATGGTAGAGATCATGATCGATCTCTAGAAAGTCTTAAAAATGTGTCTATAATA
TTTATCTAAATTTTACCTATAATTATCTACCATCTCTAGTACTAGCTAGAGATCTTTCAGAATTTTTACACAGATATTAT

CATAGGTTTGTAGATGAACAATACTTGTTTAAGCTACGTAATATGATTAGGAAAAACCATAAAATTGTACTGATATCAGA
GTATCCAAACATCTACTTGTTATGAACAAATTCGATGCATTATACTAATCCTTTTTGGTATTTTAACATGACTATAGTCT

TATTAGATCGCTAAGAGGAAAAGAACCTACTAGCGAGGACCTATTACACGATTACGCGTTGCAGAATCAAATGGTAAGCA
ATAATCTAGCGATTCTCCTTTTCTTGGATGATCGCTCCTGGATAATGTGCTAATGCGCAACGTCTTAGTTTACCATTCGT

TTCTTAAACCAATAGCATCGAGCCTGAAATGGAGATGTCCGTTTCCGGATCAGTGGATAAGAGACTTTTACATTCCTTGT
AAGAATTTGGTTATCGTAGCTCGGACTTTACCTCTACAGGCAAAGGCCTAGTCACCTATTCTCTGAAAATGTAAGGAACA

GGAGATGAGTTT
CCTCTACTCAAA

FIGURE 6 cont.

Amino acid sequence alignment of rat PAP from VIR501 with human PAP from VIR502

Boxed: Identical amino acid

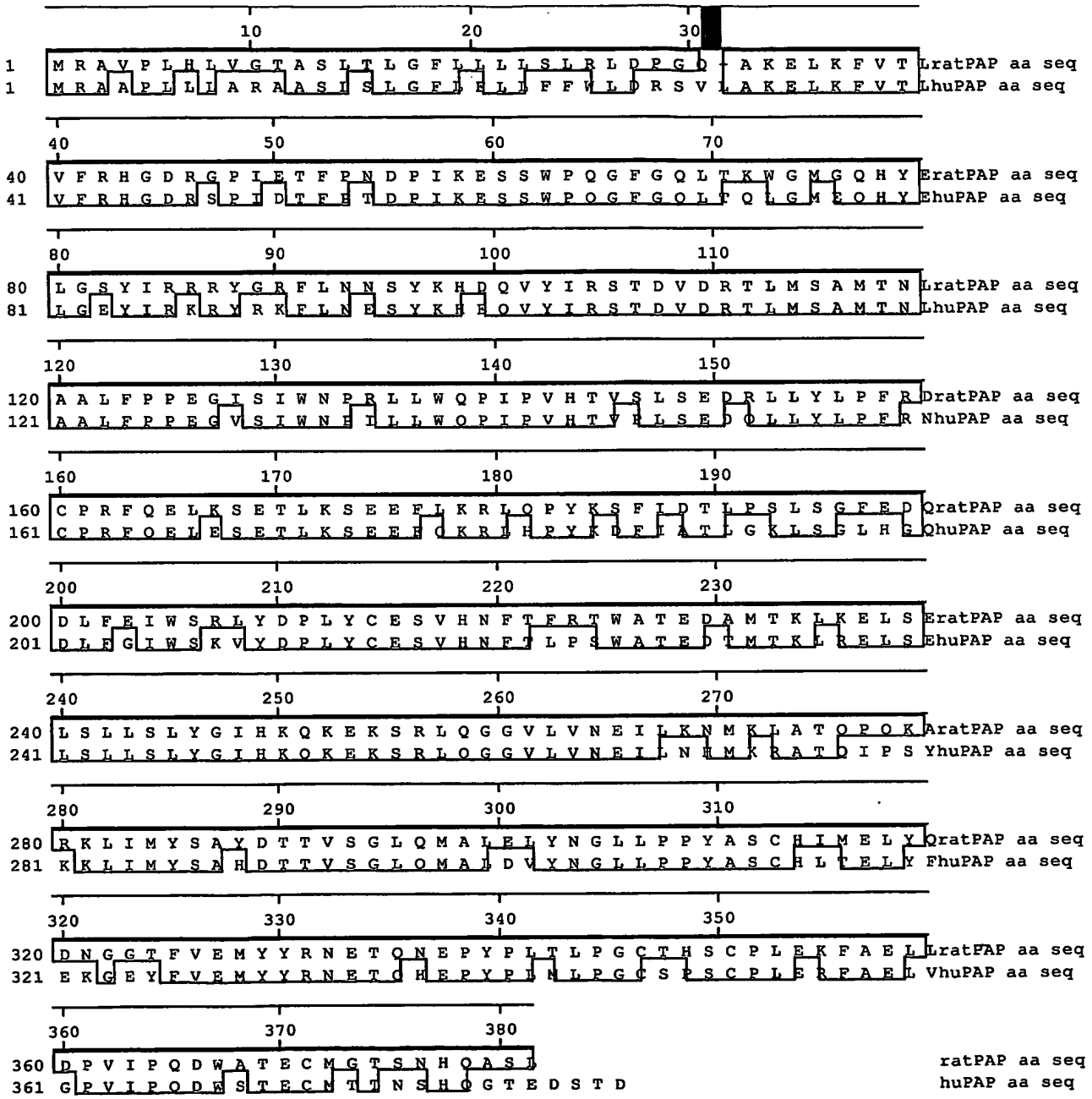


FIGURE 7

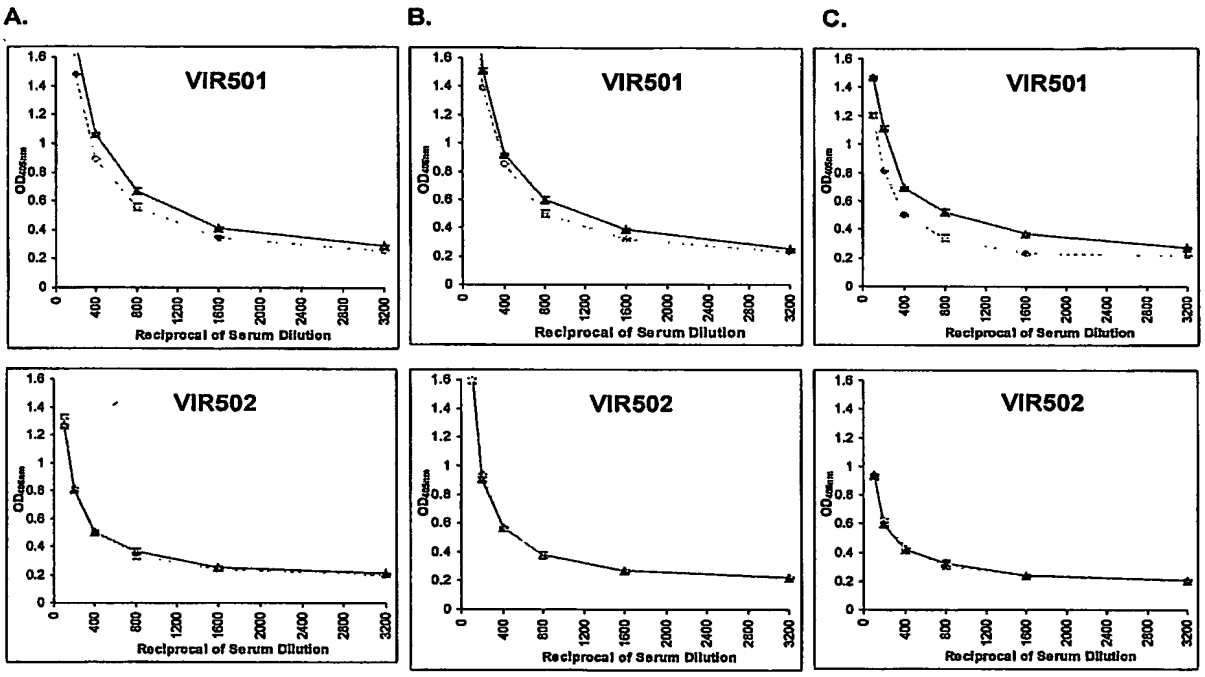


FIGURE 8

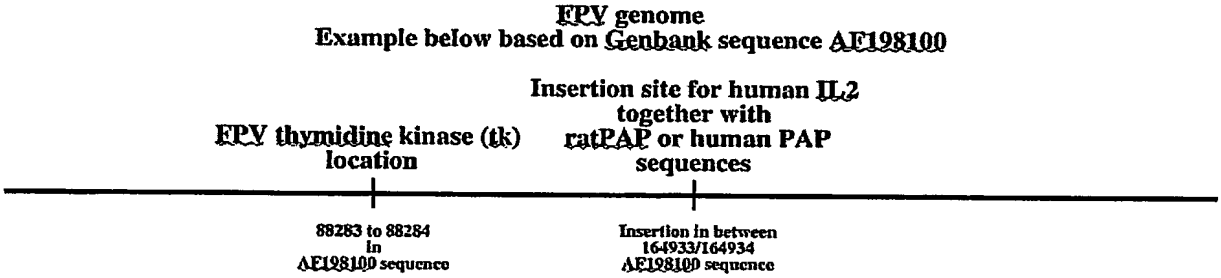
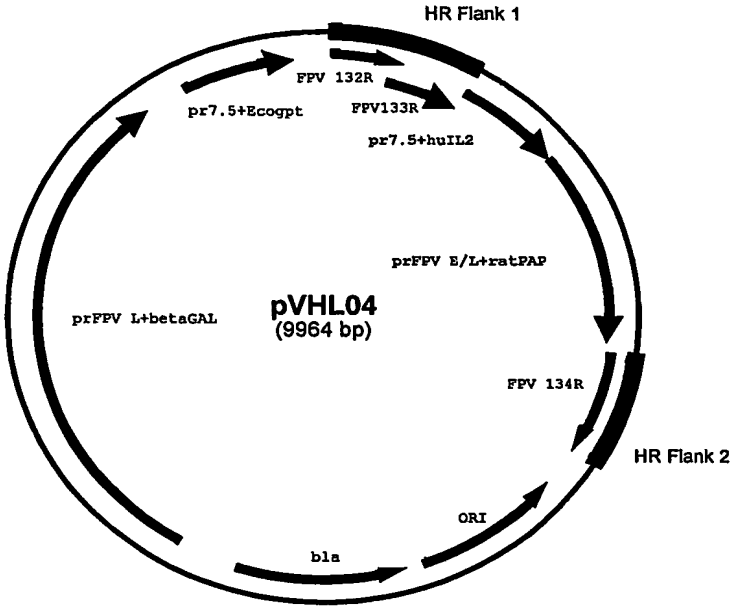

FPV genome
Example below based on Genbank sequence AF198100
Insertion site for human IL2 together with ratPAP or human PAP sequences
FPV thymidine kinase (tk) location
88283 to 88284 in AF198100 sequence
Insertion in between 164933/164934 AF198100 sequence

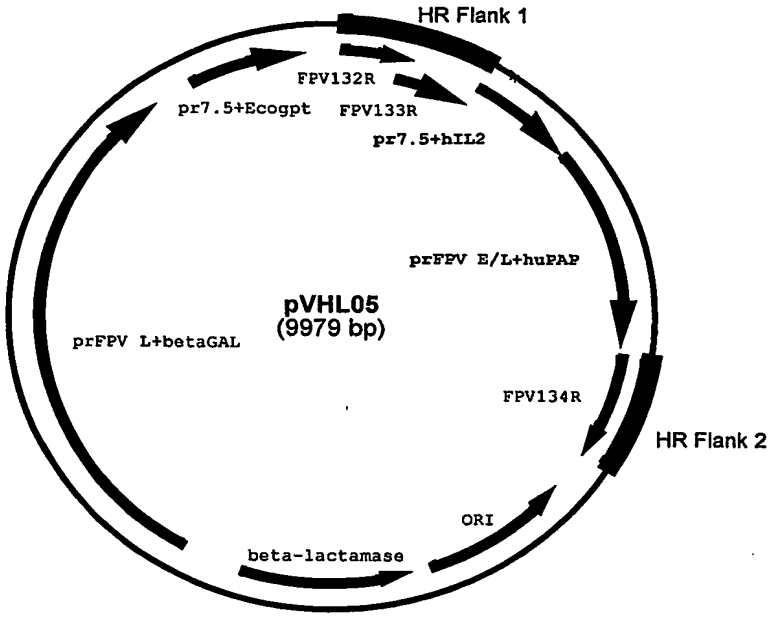
FIGURE 9



pVHL04 was constructed by cloning the following into a bacterial plasmid vector:

1. prFPV L+betaGAL: beta-Galactosidase protein coding sequence operatively linked to a fowlpox virus late promoter
2. pr7.5+Ecogpt: E coli xanthine-guanine phosphoribosyl transferase protein coding sequence operatively linked to a vaccinia virus p7.5 promoter
3. Fowlpox Virus nucleotide sequence spanning ORFs 132 and 133 – these two ORFs over lap each other. This sequence forms the homologous recombination flank 1.
4. pr7.5+huIL2: human IL2 protein coding sequence operatively linked to a vaccinia virus p7.5 promoter.
5. prFPV E/L+rat PAP: rat prostatic acid phosphatase (PAP) protein coding sequence operatively linked to a fowlpox virus early late promoter.
6. Fowlpox Virus nucleotide sequence spanning ORFs 134 - this sequence forms the homologous recombination flank 2.

FIGURE 10



pVHL05 was constructed by cloning the following into a bacterial plasmid vector:

7. prFPV L+betaGAL: beta-Galactosidase protein coding sequence operatively linked to a fowlpox virus late promoter
8. pr7.5+Ecogpt: E coli xanthine-guanine phosphoribosyl transferase protein coding sequence operatively linked to a vaccinia virus p7.5 promoter
9. Fowlpox Virus nucleotide sequence spanning ORFs 132 and 133 – these two ORFs over lap each other. This sequence forms the homologous recombination flank 1.
10. pr7.5+huIL2: human IL2 protein coding sequence operatively linked to a vaccinia virus p7.5 promoter.
11. prFPV E/L+huPAP: human prostatic acid phosphatase (PAP) protein coding sequence operatively linked to a fowlpox virus early late promoter.
12. Fowlpox Virus nucleotide sequence spanning ORFs 134 - this sequence forms the homologous recombination flank 2.

FIGURE 11